

Notice of Allowability

Application No.

10/525,608

Examiner

Jason M. Nolan, Ph.D.

Applicant(s)

GIELEN-HAERTWIG ET AL.

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 02/25/2005.
2. ☒ The allowed claim(s) is/are 1-15, 17 and 21 (now 1-17).
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some* c) ☐ None of the:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached.
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|---|
| 1. <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____ |
| 3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date <u>02/25/2005</u> | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____ |

DETAILED ACTION

Claims 1-15, 17 & 21 are currently pending in the instant application; of which, all are Currently Amended in the Preliminary Amendment, filed 02/15/2005. **Claims 16 & 18-20** are canceled.

Priority

This application is a 371 of PCT/EP2003/009108, filed on 8/18/2003. Receipt of United Kingdom 0221143.1, filed on 09/12/2002 and United Kingdom 0219894.3, filed on 08/27/2002, submitted under 35 U.S.C. §§ 119(a)-(d) is acknowledged; which papers have been placed of record in the file. Claim for priority in the Oath and ADS is acknowledged.

Information Disclosure Statement

Applicants' information disclosure statement (IDS), filed on 02/15/2005 has been considered. Please refer to Applicants' copy of the 1449 submitted herein.

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

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Authorization for this examiner's amendment was given in a telephone interview with William Gray on January 26, 2007.

The application has been amended as follows:

1. In **Claim 1**, page 5: after "Y¹, Y², Y³, Y⁴ and Y⁵ independently from each other represent CH or N, wherein the ring contains either 0, 1, or 2 nitrogen atoms," and before "or a salt thereof.", insert - - with the understanding that in this context CH also stands for a ring carbon atom, which is substituted with a substituent R³ or R⁷, - -.
2. In **Claim 2**, page 8: after "Y¹, Y², Y³, Y⁴ and Y⁵ independently from each other represent CH or N, wherein the ring contains either 0, 1, or 2 nitrogen atoms" and before *the period*, insert - - , with the understanding that in this context CH also stands for a ring carbon atom, which is substituted with a substituent R³ or R⁷. - -.
3. In **Claim 3**, page 10: after "and Y¹, Y², Y³, Y⁴ and Y⁵ each represent CH," and before *the period*, insert - - , with the understanding that in this context CH also stands for a ring carbon atom, which is substituted with a substituent R³ or R⁷. - -.
4. In **Claim 4**, page 11: after "and Y¹, Y², Y³, Y⁴ and Y⁵ each represent CH," and before *the period*, insert - - , with the understanding that in this context CH also stands for a ring carbon atom, which is substituted with a substituent R³ or R⁷. - -.
5. In **Claim 14**, page 13, after "respectively, as defined in " and before "wherein..." delete "Claims 1 and 13" and insert - - Claim 1 or 13 - -.
6. In **Claim 21**, page 17, after "amount of as least one compound according to" and before *the period*, delete "any of Claims 1 or 13" and insert - - Claim 1 or 13 - -.

Statement of Reasons for Allowance

The present invention pertains to the pyridones of formula (I) in **Claim 1** and methods of using these compounds (or compositions) for the treatment of chronic obstructive pulmonary disease (COPD), acute coronary syndrome, acute myocardial infarction or development of heart failure in humans. The compounds according to formula I are free of the prior art; nothing known in the art anticipates or renders the compounds of the instant application obvious. The closest prior art related to the formula I are the compounds shown in Schemes I, II, & III and Figure 3 of Palomo *et al.* (*J. Org. Chem.* **1991**, 56, 4418-4428).

The pyridones of formula I are shown to be inhibitors of human neutrophil elastase activity (HNE) in the specification, pp. 35-41, (see biological assays and *in vivo* model studies therein). The biological mechanisms and strategies for the inhibition of serine proteases have been well studied in the art. The review by Walker *et al.* (*CMLS, Cell. Mol. Life Sci.* **2001**, 58, 596-624) discloses multiple examples of serine protease inhibitors based on heterocyclic structures (p. 609). Another review by Chughtai *et al.* (*Journal of Aerosol Medicine* **2004**, 17(4), 289-298) discusses the role of HNE in treating diseases of the airway. Further, small molecule protease inhibitors have been well studied in the Clinic, as reviewed by Abbenante *et al.* (*Medicinal Chemistry*, **2005**, 1, 71-104). Specifically, elastase is discussed in section 2.4, pp. 77-78.

One skilled in the art would be enabled to make and use the compounds taught herein for the purpose of treating the cancers listed above using the teachings of the specification in conjunction with the teachings in the prior art.

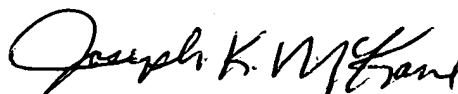
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Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jason M. Nolan, Ph.D.** whose telephone number is **(571) 272-4356** and electronic mail is **Jason.Nolan@uspto.gov**. The examiner can normally be reached on Mon - Fri (9:00 - 5:30PM). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph M^cKane** can be reached on **(571) 272-0699**. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Jason M. Nolan, Ph.D.
Examiner
Art Unit 1626



Joseph K. M^cKane
Supervisory Patent Examiner
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Date: January 26, 2007